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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/029,413	12/20/2001	Nadia Malouf	421/29/2	3695

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/029,413	MALOUF ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *1-7,12,18-33,38-41 and 43-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11,13-17,34-37 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/17/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparison A, b.*

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group XXI in the reply filed 6/8/2004 is acknowledged. The traversal is on the ground(s) that there would not be a burden to search SEQ ID NO: 1-8, 28, 29. In reply to this argument, SEQ ID NO: 1-8, 28, 29 will be searched together.

The requirement is still deemed proper and is therefore made FINAL.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

Claim Objections

Claims 8 and 42 are objected to because of the following informalities: They are dependent on non-elected claims. Appropriate correction is required.

Claim Rejections - 35 USC § § 101, 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-17, 34-37, 42 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed patentable utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance. The claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Novel biological molecules lack well-established utility and must undergo extensive experimentation. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

It is clear from the instant specification that the nucleic acid encoding the VDCC-α1 polypeptide has been assigned a function because of its similarity to known proteins (Specification at 18, Table 1). However, it is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors (Doerks et al.1998). These errors can be due to sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity because active site residues of the characterized family were not conserved (Doerks et al. page 248, column 3, fourth and fifth paragraphs). Inaccurate use of sequence-to-function methods have led to significant function-annotation errors in the sequence databases (Doerks et al. page 250, column 1, third paragraph). Furthermore, Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often

assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

The specification asserts several allegedly patentable utilities for the claimed nucleic acid encoding VDCC-α1 polynucleotide. The Specification asserts that the nucleic acid of the instant application can be used in diagnostic assays to detect VDCC-α1 polypeptide or mRNA expression in a biological sample (Specification at 6). However, this asserted utility is substantial but not specific. Hybridization probes can be designed from any polynucleotide sequence. Further, the specification does not disclose specific cDNA or DNA targets.

The specification further asserts that the nucleic acid of the instant application can be used in screening assays to identify agents which modulate VDCC-α1 receptor signal activity, VDCC-α1 ligands, or levels of mRNA encoding VDCC-α1 (Specification at 7). However, this asserted utility is not specific or substantial. Such assays can be performed with any polynucleotide. Nothing is disclosed about how the polynucleotide is affected by the compounds, which in turn affect production of mRNA and polypeptide. Additionally, the specification discloses nothing specific or substantial for the mRNA and polypeptide produced in this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

After complete characterization, this protein may be found to have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson,* 148 USPQ 689 (Sup. Ct., 1966), in

which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 USC § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a nucleic acid encoding a polypeptide which has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as VDCC-α1, the instant invention is incomplete. The polypeptide encoded by the nucleic acids of the instant invention is known to be structurally analogous to proteins that are known in the art as voltage dependent calcium channels. In the absence of knowledge of the natural substrate or biological significance of this

flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Additionally, Yan et al. teaches that in certain cases, a change of only two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another (Yan et al., Two-amino acid molecular switch in an epithelial morphogen that regulates binding to two distinct receptors. *Science* 290: 523-527, 2000). Since the claims encompass nucleic acids encoding variant polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Here, the claims do not set forth a functional limitation for the encoded variant polypeptides. Since the amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polynucleotides and encoded polypeptides which the specification only teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to make and use the claimed polypeptides. Since the claims do not enable one of skill in the art to make and use the claimed polypeptides, but only teaches how to screen for the claimed polypeptides, and since detailed information

protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which inhibit its activity is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real world" use for VDCC-α1 then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 USC § 101 as being useful.

Claims 8-17, 34-37, 42 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if, *arguendo*, a patentable utility is found for the claimed nucleic acid, claims 8-11, 13-17, 34-37, 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, which would be enabling for a nucleic acid of SEQ ID NO: 1, or a nucleic acid encoding a full-length polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for a nucleic acid encoding a polypeptide which is substantially identical to SEQ ID NO: 2, or a nucleic acid encoding a polypeptide cross-reactive with a polypeptide of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to nucleic acids encoding a polypeptide which is substantially identical to SEQ ID NO: 2, or nucleic acids encoding a polypeptide cross-reactive with a polypeptide of SEQ ID NO: 2. The claims are overly broad since insufficient guidance is

provided as to which of the myriad of variant polypeptides will retain the characteristics of VDCC-α1. The claims are directed to variant nucleic acids encoding variant polypeptides. However, Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible variants of VDCC-α1. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, As an example of the unpredictable effects of mutations on protein function, Mickle et al. (Mickle JE et al. Genotype-phenotype relationships in cystic fibrosis. Med Clin North Am. 2000 May;84(3):597-607) teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) (page 597). Several mutations can cause CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation, delta-F508, a single phenylalanine is deleted at position 508, giving ride to the CF phenotype. Thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (Voet et al. Biochemistry. 1990. John Wiley & Sons, Inc. pages 126-128 and 228-234) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood

regarding the structural and functional requirements of the polypeptides are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Thus, since Applicant has only taught how to test for nucleic acids encoding polypeptide variants of VDCC-α1, and has not taught how to make polypeptide variants of VDCC-α1, it would require undue experimentation of one of skill in the art to make and use the claimed nucleic acids.

Claims 8-17, 34-37, 42 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to nucleic acids encoding a polypeptide which is substantially identical to SEQ ID NO: 2, or nucleic acids encoding a polypeptide cross-reactive with a polypeptide of SEQ ID NO: 2. These are genus claims because the claims are directed to variant nucleic acids encoding variant polypeptides. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not

provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 2 is insufficient to describe the genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of polypeptides. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are

provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially" in claim 11 is a relative term that renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-17, 42 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 95/04822 (Harpold et al.).

The claims are drawn to nucleic acid molecules encoding polypeptides which are cross reactive with antibodies to SEQ ID NO: 2 or 4, these nucleic acids in a vector, and host cells comprising these nucleic acids. The Harpold reference teaches the cloning and expression of nucleic acids encoding voltage dependent calcium channels (see page 6), and these nucleic acids cloned into vectors and expressed in host cells (see page 39). The nucleic acids of Harpold et al. meet the limitations of the instant claims because the nucleic acids of Harpold are 62.7% identical to SEQ ID NO: 2 (see Sequence Comparison A, attached), and encode a protein with stretches of amino acids that are long enough to cross react with antibodies to SEQ ID NO: 2. Additionally, the Harpold reference teaches a nucleic acid which is 98.3% identical to SEQ ID NO: 4 (see Sequence Comparison B, attached), and the encoded polypeptide would cross react with antibodies to SEQ ID NO: 4.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8-10, 13-17, 34-37, 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/04822 (Harpold et al.) in view of the Stratagene catalog (1988, page 39).

The claims are drawn to nucleic acid molecules encoding polypeptides which are cross reactive with antibodies to SEQ ID NO: 2 or 4, these nucleic acids in a vector, and host cells comprising these nucleic acids. The Harpold reference teaches the cloning and expression of nucleic acids encoding voltage dependent calcium channels (see page 6), and these nucleic acids cloned into vectors and expressed in host cells (see page 39). The nucleic acids of Harpold et al. meet the limitations of the instant claims because the nucleic acids of Harpold are 62.7% identical to SEQ ID NO: 2 (see Sequence Comparison A, attached), and encode a protein with stretches of amino acids that are long enough to cross react with antibodies to SEQ ID NO: 2. Additionally, the Harpold reference teaches a nucleic acid which is 98.3% identical to SEQ ID NO: 4 (see Sequence Comparison B, attached), and the encoded polypeptide would cross react with antibodies to SEQ ID NO: 4. However, the Harpold et al. reference does not teach the use of a kit. The Stratagene catalog does teach a motivation to combine reagents of use into a kit page 39, column 1). It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the labeled nucleic acid molecule as taught by Harpold et al. into a kit as taught by Stratagene since the Stratagene catalog teaches a motivation for combining reagents of use in any assay into a kit. It states that "Each kit provides two services: 1) a variety of different regents have been assembled and premixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 1 different reagents,

each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control" (page 39, column 1).

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
August 4, 2004

JOSEPH MURPHY
PATENT EXAMINER

Sequence Comparison A
SEQ ID NO: 2

```
RESULT 9
AAR71003
ID   AAR71003 standard; protein; 2163 AA.
XX
AC   AAR71003;
XX
DT   25-MAR-2003  (revised)
DT   30-NOV-1995  (first entry)
XX
DE   Human neuronal calcium channel subunit alpha 1c-1.
XX
KW   Calcium channel subunit; antagonist; agonist; diagnosis;
KW   Lambert Eaton Syndrome.
XX
OS   Homo sapiens.
XX
PN   WO9504822-A1.
XX
PD   16-FEB-1995.
XX
PF   11-AUG-1994;   94WO-US009230.
XX
PR   11-AUG-1993;   93US-00105536.
PR   05-NOV-1993;   93US-00149097.
XX
PA   (SALK ) SALK INST BIOTECHNOLOGY IND ASSOC.
XX
PI   Harpold MM,  Ellis SB,  Williams ME,  Mccue AF,  Gillespie A;
XX
DR   WPI; 1995-090900/12.
DR   N-PSDB; AAQ84655.
XX
PT   DNA encoding human calcium channel sub-unit(s) - used for developing
PT   prods. for studying calcium channels, e.g. for obtaining agonists and
PT   antagonists.
XX
PS   Disclosure; Page 127-137; 285pp; English.
XX
CC   Numerous alpha 1c-specific cDNA clones were isolated in order to
CC   characterise the alpha 1c coding sequence, the initiation of translation
CC   and an alternatively spliced region. AAQ84655 sets forth one alpha 1c
CC   coding sequence (alpha 1c-1) and AAR71003 sets out its deduced AA
CC   sequence. AAQ87834 and AAR72607 set out another splice variant,
CC   designated alpha 1c-2. AAQ84656 encodes an alternative exon for the IV S3
CC   transmembrane domain. Other alpha 1c variants can be constructed by
CC   selecting alternative amino terminal ends in place of the ends in
CC   AAQ84655 and AAQ87834 and/or inserting the alternative exon in the
CC   appropriate location (see AAQ84655 FT). In addition, a nt. sequence (see
CC   AAQ84655 FT) can be deleted or inserted to produce an alternative alpha
CC   1c splice variant. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence 2163 AA;

  Query Match             62.7%;  Score 6045.5;  DB 2;  Length 2163;
  Best Local Similarity   59.6%;  Pred. No. 0;
  Matches 1244;  Conservative  239;  Mismatches  362;  Indels  243;  Gaps   37;

Qy          4 SSPQDEGLRKKQPKKPVPEILPRPPRALFCLTLENPLRKACISIVEWKPFETIILLTIFA 63
              || | :  :  :|||       |||||| ||||:||:|:|||||||||||| ||||||||
Db         77 SSTQRKRQQYGKPKKQGSTTATRPPRALLCLTLKNPIRRACISIVEWKPFEIIILLTIFA 136

Qy         64 NCVALAVYLPMPEDDNNSLNLGLEKLEYFFLIVFSIEAAMKIIAYGFLFHQDAYLRSGWN 123
              ||||||:|:| ||||:|: |  ||::|| |||:|::|| :|:|||| ||| :||||:|||
Db        137 NCVALAIYIPFPEDDSNATNSNLERVEYLFLIIFTVEAFLKVIAYGLLFHPNAYLRNGWN 196
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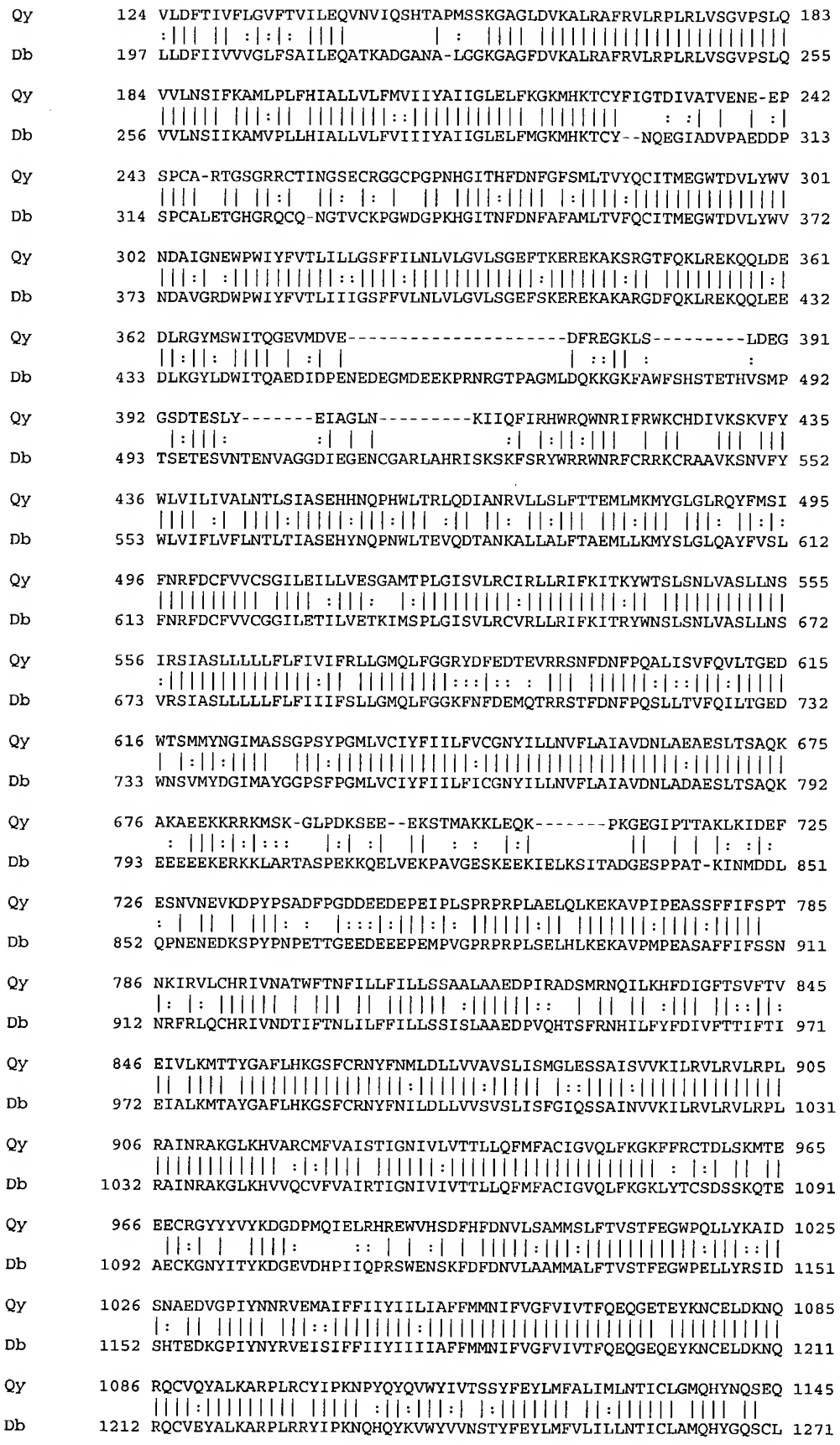

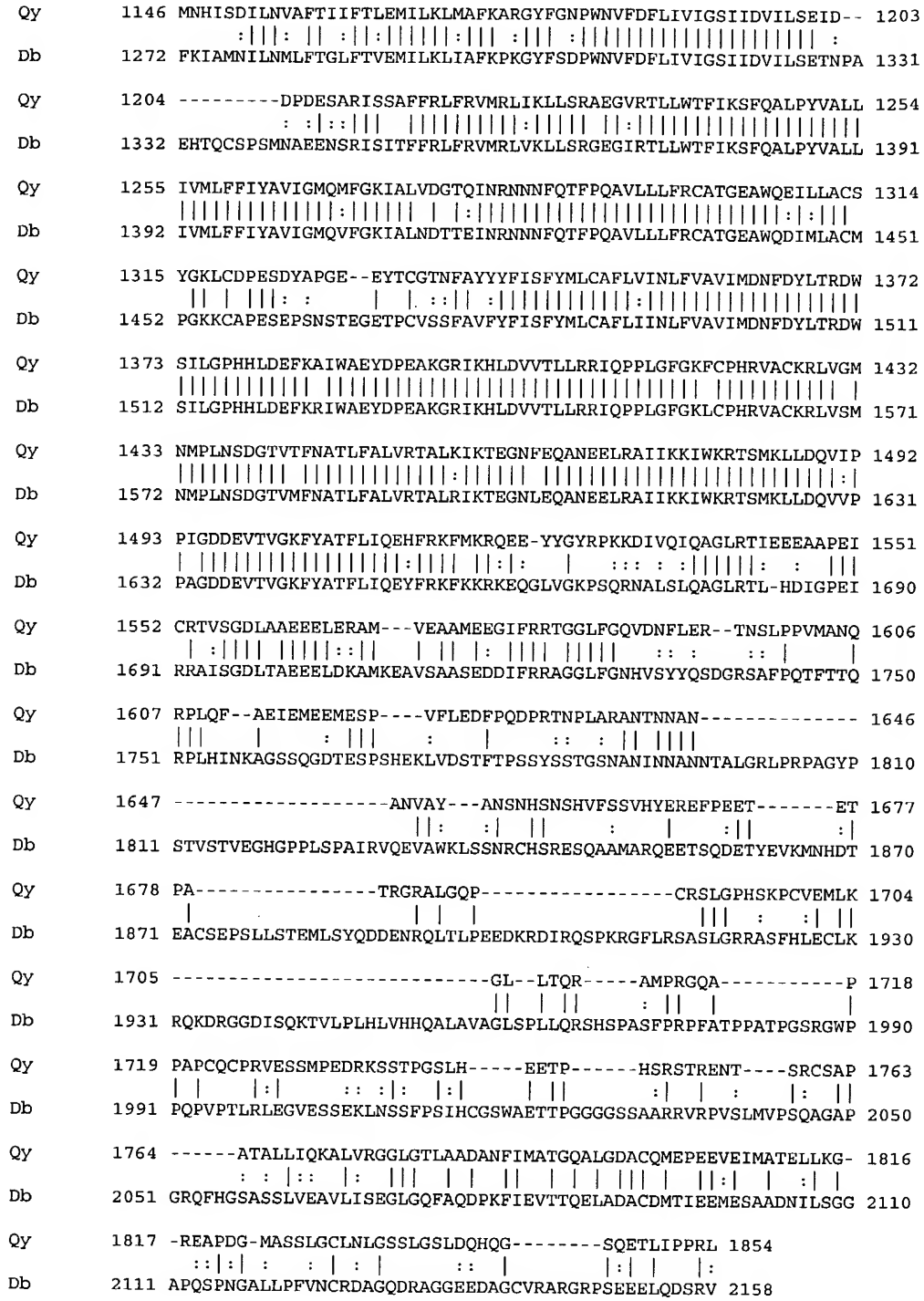

10029413 Results

SEQ ID NO: 2

Result No.	Score	Query Match	Length	DB	ID	Description
1	9644	100.0	1854	5	ABG32658	Abg32658 Human pla
2	8864.5	91.9	1873	2	AAW18390	Aaw18390 Rabbit ca
3	8864.5	91.9	1873	2	AAW37711	Aaw37711 Rabbit sk
4	8864.5	91.9	1873	3	AAY77544	Aay77544 Rabbit sk
5	8858.5	91.9	1873	2	AAR73055	Aar73055 Rabbit sk
6	8837.5	91.6	1873	1	AAP95645	Aap95645 Rabbit se
7	6054.5	62.8	2163	3	AAB10570	Aab10570 Human cal
8	6054.5	62.8	2163	5	AAE24783	Aae24783 Human cal
9	6045.5	62.7	2163	2	AAR71003	Aar71003 Human neu
10	6025	62.5	2138	2	AAR72607	Aar72607 Human neu
11	6025	62.5	2138	3	AAB10593	Aab10593 Human cal
12	6025	62.5	2138	5	AAE24805	Aae24805 Human cal
13	5998	62.2	2166	5	ABG32659	Abg32659 Human pla
14	5996.5	62.2	2157	5	ABB78220	Abb78220 Alpha1C s
15	5982.5	62.0	2161	2	AAR71002	Aar71002 Human neu

RESULT 2
AAW18390
ID AAW18390 standard; protein; 1873 AA.
XX
AC AAW18390;
XX
DT 25-MAR-2003 (revised)
DT 05-AUG-1997 (first entry)
XX
DE Rabbit calcium channel alpha-1 subunit.
XX
KW Rabbit; skeletal muscle; calcium channel; alpha-2; subunit; alpha-1;
KW transformation; reporter gene; screening assay; agonist; antagonist.
XX
OS Oryctolagus cuniculus.
XX

FH	Key	Location/Qualifiers
FT	Region	52. .70
FT		/note= "Transmembrane region"
FT	Modified-site	79
FT		/note= "N-linked glycosylation site"
FT	Region	89. .108
FT		/note= "Transmembrane region"
FT	Region	121. .139
FT		/note= "Transmembrane region"
FT	Region	161. .179
FT		/note= "Transmembrane region"
FT	Region	199. .218
FT		/note= "Transmembrane region"
FT	Modified-site	257
FT		/note= "N-linked glycosylation site"
FT	Region	310. .334
FT		/note= "Transmembrane region"
FT	Region	433. .451
FT		/note= "Transmembrane region"
FT	Region	467. .486
FT		/note= "Transmembrane region"
FT	Region	495. .513
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FT	Region	524. .542
FT		/note= "Transmembrane region"
FT	Region	562. .581
FT		/note= "Transmembrane region"
FT	Region	637. .661
FT		/note= "Transmembrane region"
FT	Modified-site	687
FT		/note= "Potential cAMP-dependent phosphorylation site"

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FT   Modified-site   797
FT                   /note= "N-linked glycosylation site"
FT   Region          800. .818
FT                   /note= "Transmembrane region"
FT   Region          835. .854
FT                   /note= "Transmembrane region"
FT   Region          893. .912
FT                   /note= "Transmembrane region"
FT   Region          931. .950
FT                   /note= "Transmembrane region"
FT   Region          967. .885
FT                   /note= "Transmembrane region"
FT   Region          1041. .1065
FT                   /note= "Transmembrane region"
FT   Region          1119. .1137
FT                   /note= "Transmembrane region"
FT   Region          1153. .1172
FT                   /note= "Transmembrane region"
FT   Region          1181. .1199
FT                   /note= "Transmembrane region"
FT   Region          1232. .1250
FT                   /note= "Transmembrane region"
FT   Region          1270. .1289
FT                   /note= "Transmembrane region"
FT   Region          1357. .1381
FT                   /note= "Transmembrane region"
FT   Modified-site   1464
FT                   /note= "N-linked glycosylation site"
FT   Modified-site   1502
FT                   /note= "Potential cAMP-dependent phosphorylation site"
FT   Modified-site   1552
FT                   /note= "Potential cAMP-dependent phosphorylation site"
FT   Modified-site   1575
FT                   /note= "Potential cAMP-dependent phosphorylation site"
FT   Modified-site   1674
FT                   /note= "N-linked glycosylation site"
FT   Modified-site   1757
FT                   /note= "Potential cAMP-dependent phosphorylation site"
FT   Modified-site   1772
FT                   /note= "Potential cAMP-dependent phosphorylation site"
FT   Modified-site   1854
FT                   /note= "Potential cAMP-dependent phosphorylation site"
XX
PN   US5618720-A.
XX
PD   08-APR-1997.
XX
PF   15-FEB-1995;   95US-00404354.
XX
PR   04-APR-1988;   88US-00176899.
PR   04-APR-1989;   89WO-US001408.
PR   08-NOV-1990;   90US-00603751.
PR   13-JUL-1992;   92US-00914231.
PR   28-SEP-1994;   94US-00314083.
XX
PA   (SIBI-) SIBIA NEUROSCIENCES INC.
XX
PI   Schwartz A,  Williams ME,  Brenner R,  Harpold MM,  Ellis SB;
XX
DR   WPI; 1997-225431/20.
DR   N-PSDB; AAT70228.
XX
PT   Eukaryotic cell expressing heterologous calcium channel - comprising
PT   alpha-1 and alpha-2 sub:units; used in drug screening assays.
XX
PS   Claim 3; Col 17-30; 50pp; English.
XX
CC   This sequence represents the rabbit skeletal muscle calcium channel alpha
CC   -1 subunit. This protein comprises twenty-four potential transmembrane
CC   regions and has a molecular weight of 212143. The protein contains four
CC   internal repeated segments. Each repeat comprises five hydrophobic
```

CC segments and one segment with strong positive charge. The alpha-1 protein
CC lacks a hydrophobic amino terminal sequence characteristic of a signal
CC peptide and it is thought that the four internal repeats represent the 24
CC transmembrane segments and that the N- and C-termini are extracellular.
CC This sequence may be used, in conjunction with the alpha-2 subunit coding
CC sequence (see also AAT70227) to transform a eukaryotic cell. The cell may
CC be used optionally with a reporter gene, in screening assays for Ca2+
CC channel agonists or antagonists. (Updated on 25-MAR-2003 to correct PF
CC field.) (Updated on 25-MAR-2003 to correct PR field.)
XX
SQ Sequence 1873 AA;

Query Match 91.9%; Score 8864.5; DB 2; Length 1873;
Best Local Similarity 91.2%; Pred. No. 0;
Matches 1707; Conservative 58; Mismatches 88; Indels 19; Gaps 1;

```
Qy          1 MEPSSPQDEGLRKKQPKKPVPEILPRPPRALFCLTLENPLRKACISIVEWKPFETIILLT 60
              |||||||||||||||||||:||:|||||||||||||:||||||||||||||||||||||
Db          1 MEPSSPQDEGLRKKQPKKPLPEVLPRPPRALFCLTLQNPLRKACISIVEWKPFETIILLT 60

Qy         61 IFANCVALAVYLPMPEDDNNSLNLGLEKLEYFFLIVFSIEAAMKIIAYGFLFHQDAYLRS 120
              |||||||||||||||||||||||||||||||| |||||||||||||||||||||||||||
Db         61 IFANCVALAVYLPMPEDDNNSLNLGLEKLEYFFLTVFSIEAAMKIIAYGFLFHQDAYLRS 120

Qy        121 GWNVLDFTIVFLGVFTVILEQVNVIQSHTAPMSSKGAGLDVKALRAFRVLRPLRLVSGVP 180
              ||||||| |||||||| ||||||||||:||||||||||||||||||||||||||||||||
Db        121 GWNVLDFIIVFLGVFTAILEQVNVIQSNTAPMSSKGAGLDVKALRAFRVLRPLRLVSGVP 180

Qy        181 SLQVVLNSIFKAMLPLFHIALLVLFMVIIYAIIGLELFKGKMHKTCYFIGTDIVATVENE 240
              ||||||||||||||||||||||||||||||||||||||||||||||:||||||||||||
Db        181 SLQVVLNSIFKAMLPLFHIALLVLFMVIIYAIIGLELFKGKMHKTCYYIGTDIVATVENE 240

Qy        241 EPSPCARTGSGRRCTINGSECRGGCPGPNHGITHFDNFGFSMLTVYQCITMEGWTDVLYW 300
              :|||||||||||| |||||||||| ||||||||||||||||||||||||||||||||||
Db        241 KPSPCARTGSGRPCTINGSECRGGWPGPNHGITHFDNFGFSMLTVYQCITMEGWTDVLYW 300

Qy        301 VNDAIGNEWPWIYFVTLILLGSFFILNLVLGVLSGEFTKEREKAKSRGTFQKLREKQQLD 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||:
Db        301 VNDAIGNEWPWIYFVTLILLGSFFILNLVLGVLSGEFTKEREKAKSRGTFQKLREKQQLE 360

Qy        361 EDLRGYMSWITQGEVMDVEDFREGKLSLDEGGSDTESLYEIAGLNKIIQFIRHWRQWNRI 420
              |||||||||||||||||| |||||||:|||||||||||| ||||||||||||||||||:
Db        361 EDLRGYMSWITQGEVMDVEDLREGKLSLEEGGSDTESLYEIEGLNKIIQFIRHWRQWNRV 420

Qy        421 FRWKCHDIVKSKVFYWLVILIVALNTLSIASEHHNQPHWLTRLQDIANRVLLSLFTTEML 480
              |||||||:|||:|||||||||||||||||||||||| ||| |||||||||||||| |||
Db        421 FRWKCHDLVKSRVFYWLVILIVALNTLSIASEHHNQPLWLTHLQDIANRVLLSLFTIEML 480

Qy        481 MKMYGLGLRQYFMSIFNRFDCFVVCSGILEILLVESGAMTPLGISVLRCIRLLRIFKITK 540
              :|||||||||||||||||||||||||||:|||||||||||||||||||||||:|||||
Db        481 LKMYGLGLRQYFMSIFNRFDCFVVCSGILELLLVESGAMTPLGISVLRCIRLLRLFKITK 540

Qy        541 YWTSLSNLVASLLNSIRSIASLLLLLFLFIVIFRLLGMQLFGGRYDFEDTEVRRSNFDNF 600
              ||||||||||||||||||||||||||||:|| |||||||||||||||||||||||||||
Db        541 YWTSLSNLVASLLNSIRSIASLLLLLFLFIIIFALLGMQLFGGRYDFEDTEVRRSNFDNF 600

Qy        601 PQALISVFQVLTGEDWTSMMYNGIMASSGPSYPGMLVCIYFIILFVCGNYILLNVFLAIA 660
              |||||||||||||||| |:||||||| ||||||:|||||||||||||||||||||||||
Db        601 PQALISVFQVLTGEDWNSVMYNGIMAYGGPSYPGVLVCIYFIILFVCGNYILLNVFLAIA 660

Qy        661 VDNLAEAESLTSAQKAKAEEKKRRKMSKGLPDKSEEEKSTMAKKLEQKPKGEGIPTTAKL 720
              ||||||||||||||||||:||||||:||||||:||||| ||||||||||||||||||||
Db        661 VDNLAEAESLTSAQKAKAEERKRRKMSRGLPDKTEEEKSVMAKKLEQKPKGEGIPTTAKL 720

Qy        721 KIDEFESNVNEVKDPYPSADFPGDDEEDEPEIPLSPRPRPLAELQLKEKAVPIPEASSFF 780
              |:|||||||||||||||||||||||||||:|||||||||||||||||||||||||||||
Db        721 KVDEFESNVNEVKDPYPSADFPGDDEEDEPEIPVSPRPRPLAELQLKEKAVPIPEASSFF 780

Qy        781 IFSPTNKIRVLCHRIVNATWFTNFILLFILLSSAALAAEDPIRADSMRNQILKHFDIGFT 840
              |||||||:|||||||||||||||||||||||||||||||:|:||||| :||| ||
Db        781 IFSPTNKVRVLCHRIVNATWFTNFILLFILLSSAALAAEDPIRAESVRNQILGYFDIAFT 840
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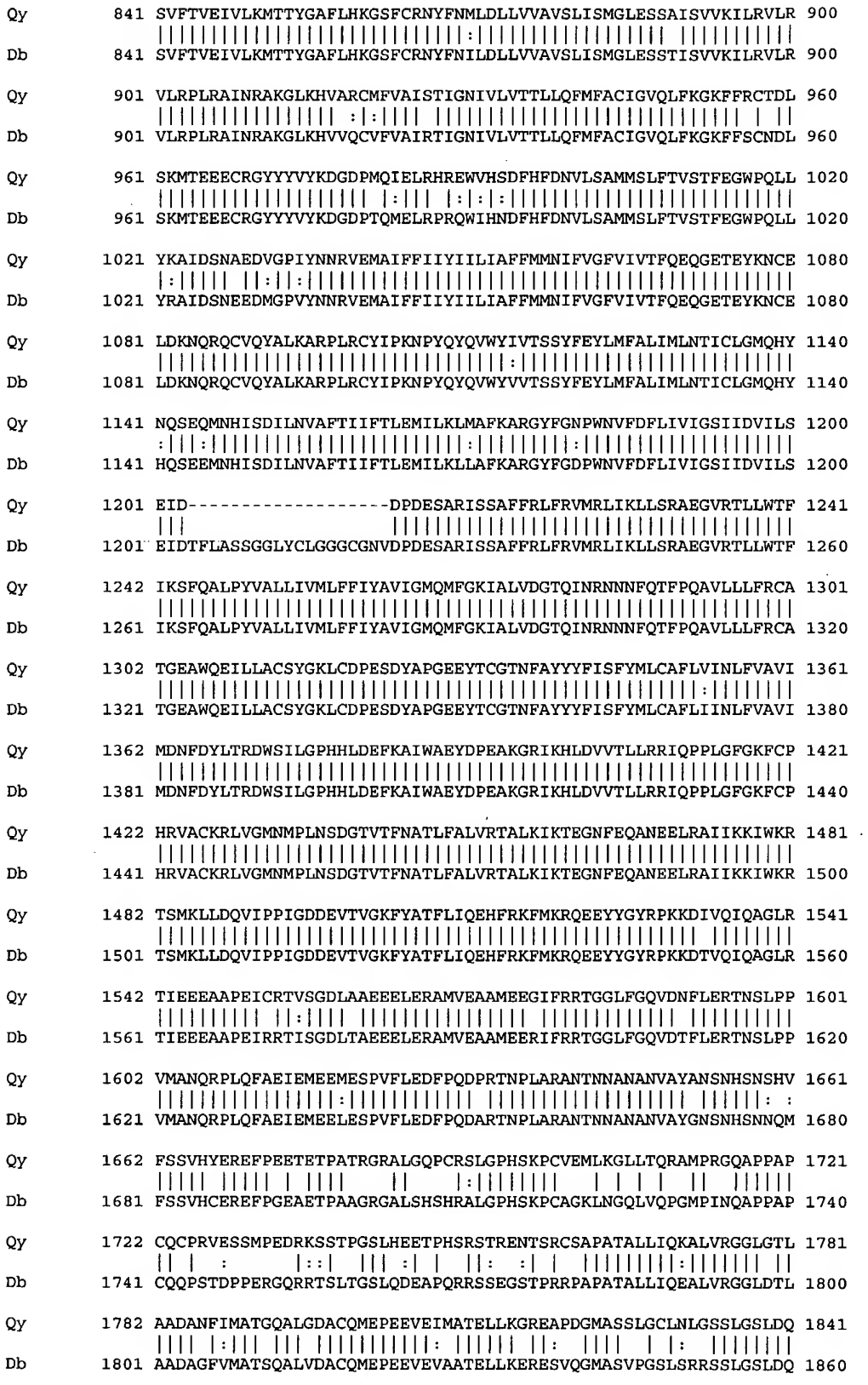

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Db       1861 VQGSQETLIPPR 1872


RESULT 6
AAP95645
ID   AAP95645 standard; protein; 1873 AA.
XX
AC   AAP95645;
XX
DT   27-AUG-2003  (revised)
DT   25-MAR-2003  (revised)
DT   21-MAR-1990  (first entry)
XX
DE   Rabbit seletal muscle alpha-1 sub-unit gene product.
XX
KW   Skeletal muscle.
XX
OS   Sylvilagus sp.
XX
PN   WO8909834-A.
XX
PD   19-OCT-1989.
XX
PF   04-APR-1989;   89WO-US001408.
XX
PR   04-APR-1988;   88US-00176899.
XX
PA   (SALK ) SALK INST BIOLOGICAL STUDIES.
XX
PI   Ellis SB,  Williams ME,  Harpold MM,  Schwartz A,  Sartor J;
XX
DR   WPI; 1989-324236/44.
DR   N-PSDB; AAN91778.
XX
PT   New DNA encoding alpha-2 sub-unit of animal calcium channel - also new
PT   protein product and eukaryotic cells for testing cpds. for calcium
PT   agonist or antagonist activity.
XX
PS   Disclosure; Page 16-1 to 18-3; 68pp; English.
XX
CC   Also used to diagnose Lambert-Eaton syndrome by reacting test serum with
CC   alpha-1 and alpha-2 subunits. Labelled fragments can be used as probes.
CC   (Updated on 25-MAR-2003 to correct PF field.) (Updated on 25-MAR-2003 to
CC   correct PA field.) (Updated on 27-AUG-2003 to correct OS field.)
XX
SQ   Sequence 1873 AA;

  Query Match             91.6%;  Score 8837.5;  DB 1;  Length 1873;
  Best Local Similarity   90.9%;  Pred. No. 0;
  Matches 1702;  Conservative   59;  Mismatches   92;  Indels   19;  Gaps    1;

Qy          1 MEPSSPQDEGLRKKQPKKPVPEILPRPPRALFCLTLENPLRKACISIVEWKPFETIILLT 60
              |||||||||||||||||||:||:||||||||||||:|||||||||||||||||||||||
Db          1 MEPSSPQDEGLRKKQPKKPLPEVLPRPPRALFCLTLQNPLRKACISIVEWKPFETIILLT 60

Qy         61 IFANCVALAVYLPMPEDDNNSLNLGLEKLEYFFLIVFSIEAAMKIIAYGFLFHQDAYLRS 120
              |||||||||||||||||||||||||||||||| |||||||||||||||||| ||||
Db         61 IFANCVALAVYLPMPEDDNNSLNLGLEKLEYFFLTVFSIEAAMKIIAYGFLFHQDGYLRS 120

Qy        121 GWNVLDFTIVFLGVFTVILEQVNVIQSHTAPMSSKGAGLDVKALRAFRVLRPLRLVSGVP 180
              ||||||| |||||||| |||||||||:||||||||||||||||||||||||||||||||
Db        121 GWNVLDFIIVFLGVFTAILEQVNVIQSNTAPMSSKGAGLDVKALRAFRVLRPLRLVSGVP 180

Qy        181 SLQVVLNSIFKAMLPLFHIALLVLFMVIIYAIIGLELFKGKMHKTCYFIGTDIVATVENE 240
              |||||||||||||||||||||||||||||||||||||||||||||||:||||||||||||
Db        181 SLQVVLNSIFKAMLPLFHIALLVLFMVIIYAIIGLELFKGKMHKTCYYIGTDIVATVENE 240

Qy        241 EPSPCARTGSGRRCTINGSECRGGCPGPNHGITHFDNFGFSMLTVYQCITMEGWTDVLYW 300
              :|||||||||||| |||||||||| ||||||||||||||||||||||||||||||||||
Db        241 KPSPCARTGSGRPCTINGSECRGGWPGPNHGITHFDNFGFSMLTVYQCITMEGWTDVLYW 300
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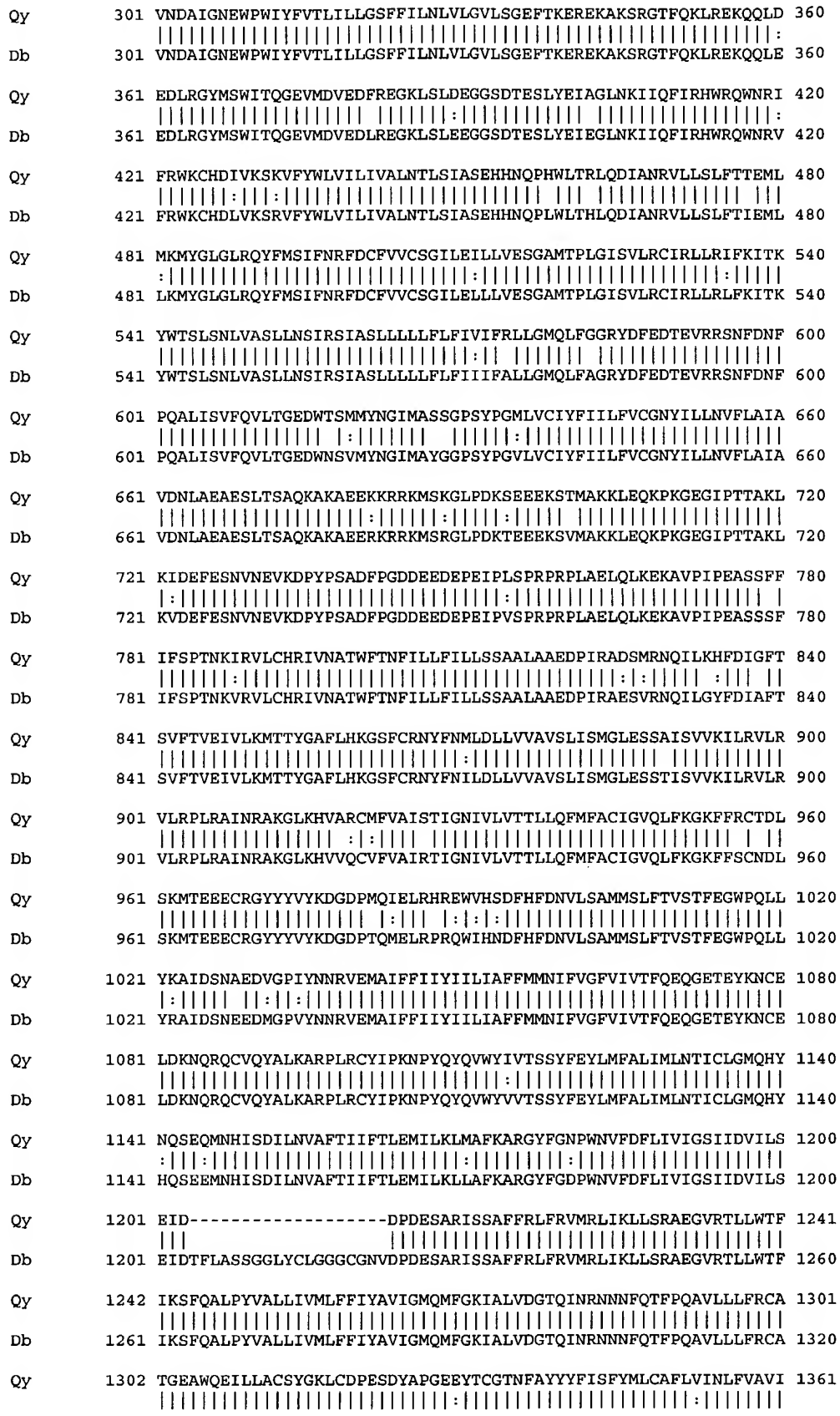

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Db       1321 TGEAWQEILLACSYGKLCDPESDYAPGEDYTCGTNFAYYYFISFYMLCAFLIINLFVAVI 1380

Qy       1362 MDNFDYLTRDWSILGPHHLDEFKAIWAEYDPEAKGRIKHLDVVTLLRRIQPPLGFGKFCP 1421
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 MDNFDYLTRDWSILGPHHLDEFKAIWAEYDPEAKGRIKHLDVVTLLRRIQPPLGFGKFCP 1440

Qy       1422 HRVACKRLVGMNMPLNSDGTVTFNATLFALVRTALKIKTEGNFEQANEELRAIIKKIWKR 1481
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 HRVACKRLVGMNMPLNSDGTVTFNATLFALVRTALKIKTEGNFEQANEELRAIIKKIWKR 1500

Qy       1482 TSMKLLDQVIPPIGDDEVTVGKFYATFLIQEHFRKFMKRQEEYYGYRPKKDIVQIQAGLR 1541
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 TSMKLLDQVIPPIGDDEVTVGKFYATFLIQEHFRKFMKRQEEYYGYRPKKDTVQIQAGLR 1560

Qy       1542 TIEEEAAPEICRTVSGDLAAEEELERAMVEAAMEEGIFRRTGGLFGQVDNFLERTNSLPP 1601
             |||||||||| ||:|||| |||||||||||||||| |||||||||||| ||||||||||
Db       1561 TIEEEAAPEIRRTISGDLTAEEELERAMVEAAMEERIFRRTGGLFGQVDTFLERTNSLPP 1620

Qy       1602 VMANQRPLQFAEIEMEEMESPVFLEDFPQDPRTNPLARANTNNANANVAYANSNHSNSHV 1661
             ||| |||||||||||||:|||||||||||| |||||||||||||||||| ||||||: :
Db       1621 VMATQRPLQFAEIEMEELESPVFLEDFPQDARTNPLARANTNNANANVAYGNSNHSNNQM 1680

Qy       1662 FSSVHYEREFPEETETPATRGRALGQPCRSLGPHSKPCVEMLKGLLTQRAMPRGQAPPAP 1721
             ||||| ||||| | ||||    ||    |:||||||||   | | | |  ||  ||||||
Db       1681 FSSVHCEREFPGEAETPAAGRGALSHSHRALGPHSKPCAGKLNGQLVQPGMPINQAPPAP 1740

Qy       1722 CQCPRVESSMPEDRKSSTPGSLHEETPHSRSTRENTSRCSAPATALLIQKALVRGGLGTL 1781
             || |  :      |::|  ||| :| |  ||:  :| |  |||||||||:||||||| ||
Db       1741 CQQPSTDPPERGQRRTSLTGSLQDEAPQRRSSEGSTPRRPAPATALLIQEALVRGGLDTL 1800

Qy       1782 AADANFIMATGQALGDACQMEPEEVEIMATELLKGREAPDGMASSLGCLNLGSSLGSLDQ 1841
             |||| |:||| ||| ||||||||||: |||||| ||:  |||| | |:  ||||||||
Db       1801 AADAGFVMATSQALVDACQMEPEEVEVAATELLKERESVQGMASVPGSLSRRSSLGSLDQ 1860

Qy       1842 HQGSQETLIPPR 1853
              ||||||||||||
Db       1861 VQGSQETLIPPR 1872
```

```
RESULT 9
AAR71003
ID   AAR71003 standard; protein; 2163 AA.
XX
AC   AAR71003;
XX
DT   25-MAR-2003  (revised)
DT   30-NOV-1995  (first entry)
XX
DE   Human neuronal calcium channel subunit alpha 1c-1.
XX
KW   Calcium channel subunit; antagonist; agonist; diagnosis;
KW   Lambert Eaton Syndrome.
XX
OS   Homo sapiens.
XX
PN   WO9504822-A1.
XX
PD   16-FEB-1995.
XX
PF   11-AUG-1994;   94WO-US009230.
XX
PR   11-AUG-1993;   93US-00105536.
PR   05-NOV-1993;   93US-00149097.
XX
PA   (SALK ) SALK INST BIOTECHNOLOGY IND ASSOC.
XX
PI   Harpold MM,  Ellis SB,  Williams ME,  Mccue AF,  Gillespie A;
XX
DR   WPI; 1995-090900/12.
DR   N-PSDB; AAQ84655.
XX
PT   DNA encoding human calcium channel sub-unit(s) - used for developing
```

PT prods. for studying calcium channels, e.g. for obtaining agonists and
PT antagonists.
XX
PS Disclosure; Page 127-137; 285pp; English.
XX
CC Numerous alpha 1c-specific cDNA clones were isolated in order to
CC characterise the alpha 1c coding sequence, the initiation of translation
CC and an alternatively spliced region. AAQ84655 sets forth one alpha 1c
CC coding sequence (alpha 1c-1) and AAR71003 sets out its deduced AA
CC sequence. AAQ87834 and AAR72607 set out another splice variant,
CC designated alpha 1c-2. AAQ84656 encodes an alternative exon for the IV S3
CC transmembrane domain. Other alpha 1c variants can be constructed by
CC selecting alternative amino terminal ends in place of the ends in
CC AAQ84655 and AAQ87834 and/or inserting the alternative exon in the
CC appropriate location (see AAQ84655 FT). In addition, a nt. sequence (see
CC AAQ84655 FT) can be deleted or inserted to produce an alternative alpha
CC 1c splice variant. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ Sequence 2163 AA;

Query Match 62.7%; Score 6045.5; DB 2; Length 2163;
Best Local Similarity 59.6%; Pred. No. 0;
Matches 1244; Conservative 239; Mismatches 362; Indels 243; Gaps 37;

```
Qy          4 SSPQDEGLRKKQPKKPVPEILPRPPRALFCLTLENPLRKACISIVEWKPFETIILLTIFA 63
              || | :  :  :|||       |||||| ||||:||:|:|||||||||||| ||||||||
Db         77 SSTQRKRQQYGKPKKQGSTTATRPPRALLCLTLKNPIRRACISIVEWKPFEIIILLTIFA 136

Qy         64 NCVALAVYLPMPEDDNNSLNLGLEKLEYFFLIVFSIEAAMKIIAYGFLFHQDAYLRSGWN 123
              ||||||:|:| |||||:|: |  ||::|| |||:|::|| :|:|||| ||| :||||:|||
Db        137 NCVALAIYIPFPEDDSNATNSNLERVEYLFLIIFTVEAFLKVIAYGLLFHPNAYLRNGWN 196

Qy        124 VLDFTIVFLGVFTVILEQVNVIQSHTAPMSSKGAGLDVKALRAFRVLRPLRLVSGVPSLQ 183
              :||| || :|:|: ||||        | :  |||| ||||||||||||||||||||||||
Db        197 LLDFIIVVVGLFSAILEQATKADGANA-LGGKGAGFDVKALRAFRVLRPLRLVSGVPSLQ 255

Qy        184 VVLNSIFKAMLPLFHIALLVLFMVIIYAIIGLELFKGKMHKTCYFIGTDIVATVENE-EP 242
              |||||| |||:|| |||||||::|||||||||| ||||||||     : :| |  | :|
Db        256 VVLNSIIKAMVPLLHIALLVLFVIIIYAIIGLELFMGKMHKTCY--NQEGIADVPAEDDP 313

Qy        243 SPCA-RTGSGRRCTINGSECRGGCPGPNHGITHFDNFGFSMLTVYQCITMEGWTDVLYWV 301
              ||||  || ||:|  ||: |: |  || ||||:|||| |:||||:|||||||||||||||
Db        314 SPCALETGHGRQCQ-NGTVCKPGWDGPKHGITNFDNFAFAMLTVFQCITMEGWTDVLYWV 372

Qy        302 NDAIGNEWPWIYFVTLILLGSFFILNLVLGVLSGEFTKEREKAKSRGTFQKLREKQQLDE 361
              |||:| :|||||||||::|||||:|||||||||||||:|||||||:|| ||||||||||:|
Db        373 NDAVGRDWPWIYFVTLIIIGSFFVLNLVLGVLSGEFSKEREKAKARGDFQKLREKQQLEE 432

Qy        362 DLRGYMSWITQGEVMDVE--------------------DFREGKLS---------LDEG 391
              ||:||: |||| | :| |                     | ::|| :         :
Db        433 DLKGYLDWITQAEDIDPENEDEGMDEEKPRNRGTPAGMLDQKKGKFAWFSHSTETHVSMP 492

Qy        392 GSDTESLY-------EIAGLN---------KIIQFIRHWRQWNRIFRWKCHDIVKSKVFY 435
               |:|||:        :| | |            :| |:||:|||  | ||   ||| |||
Db        493 TSETESVNTENVAGGDIEGENCGARLAHRISKSKFSRYWRRWNRFCRRKCRAAVKSNVFY 552

Qy        436 WLVILIVALNTLSIASEHHNQPHWLTRLQDIANRVLLSLFTTEMLMKMYGLGLRQYFMSI 495
              |||| :| ||||:|||||:|||:||| :|| ||: ||:||| |||:||| |||: ||:|:
Db        553 WLVIFLVFLNTLTIASEHYNQPNWLTEVQDTANKALLALFTAEMLLKMYSLGLQAYFVSL 612

Qy        496 FNRFDCFVVCSGILEILLVESGAMTPLGISVLRCIRLLRIFKITKYWTSLSNLVASLLNS 555
              |||||||||| |||| :|||:  |:||||||||:||||||||:|| ||||||||||||
Db        613 FNRFDCFVVCGGILETILVETKIMSPLGISVLRCVRLLRIFKITRYWNSLSNLVASLLNS 672

Qy        556 IRSIASLLLLLFLFIVIFRLLGMQLFGGRYDFEDTEVRRSNFDNFPQALISVFQVLTGED 615
              :|||||||||||||:|| |||||||||:::|:: : ||| ||||||:|::|||:|||||
Db        673 VRSIASLLLLLFLFIIIFSLLGMQLFGGKFNFDEMQTRRSTFDNFPQSLLTVFQILTGED 732

Qy        616 WTSMMYNGIMASSGPSYPGMLVCIYFIILFVCGNYILLNVFLAIAVDNLAEAESLTSAQK 675
              | |:||:||||  |||:||||||||||||:|||||||||||||||:|||||||||
Db        733 WNSVMYDGIMAYGGPSFPGMLVCIYFIILFICGNYILLNVFLAIAVDNLADAESLTSAQK 792
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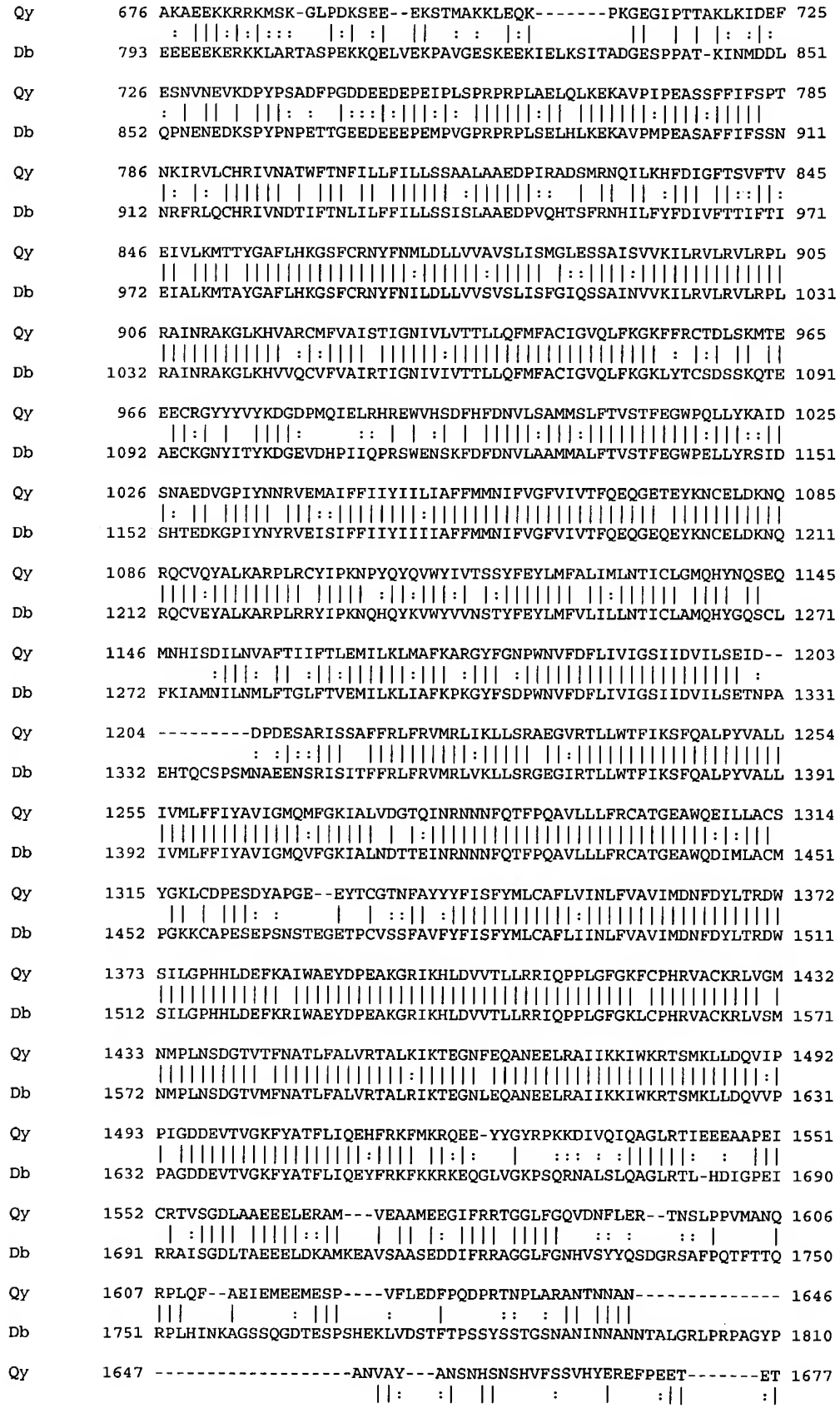

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Db       1811 STVSTVEGHGPPLSPAIRVQEVAWKLSSNRCHSRESQAAMARQEETSQDETYEVKMNHDT 1870

Qy       1678 PA----------------TRGRALGQP----------------CRSLGPHSKPCVEMLK 1704
                |                   | | |                    |||  :   :| ||
Db       1871 EACSEPSLLSTEMLSYQDDENRQLTLPEEDKRDIRQSPKRGFLRSASLGRRASFHLECLK 1930

Qy       1705 ----------------------------GL--LTQR-----AMPRGQA----------P 1718
                                          ||  | ||     : ||  |          |
Db       1931 RQKDRGGDISQKTVLPLHLVHHQALAVAGLSPLLQRSHSPASFPRPFATPPATPGSRGWP 1990

Qy       1719 PAPCQCPRVESSMPEDRKSSTPGSLH-----EETP------HSRSTRENT----SRCSAP 1763
                | |    |:|     :: :|:  |:|     | ||       :|  |  :    |:  ||
Db       1991 PQPVPTLRLEGVESSEKLNSSFPSIHCGSWAETTPGGGGSSAARRVRPVSLMVPSQAGAP 2050

Qy       1764 ------ATALLIQKALVRGGLGTLAADANFIMATGQALGDACQMEPEEVEIMATELLKG- 1816
                    : : |::  |:  |||  | |  ||  | | | ||| |  ||:|  |  :| |
Db       2051 GRQFHGSASSLVEAVLISEGLGQFAQDPKFIEVTTQELADACDMTIEEMESAADNILSGG 2110

Qy       1817 -REAPDG-MASSLGCLNLGSSLGSLDQHQG--------SQETLIPPRL 1854
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Db       2111 APQSPNGALLPFVNCRDAGQDRAGGEEDAGCVRARGRPSEEELQDSRV 2158
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SEQ ID NO: 4

Result No.	Score	% Query Match	Length	DB	ID	Description
1	11391	100.0	2166	5	ABG32659	Abg32659 Human pla
2	11373.5	99.8	2181	5	ABG61941	Abg61941 Prostate
3	11373.5	99.8	2181	7	ADB75226	Adb75226 Prostate
4	11373.5	99.8	2182	7	ADD48699	Add48699 Human Pro
5	11202.5	98.3	2161	2	AAR71002	Aar71002 Human neu
6	11202.5	98.3	2161	2	AAW63149	Aaw63149 Human cal
7	11168.5	98.0	2161	2	AAR71001	Aar71001 Human neu
8	11168.5	98.0	2161	2	AAW63137	Aaw63137 Human cal
9	11168.5	98.0	2161	3	AAB10568	Aab10568 Human cal
10	11168.5	98.0	2161	5	AAE24781	Aae24781 Human cal
11	11157.5	98.0	2161	7	ADE62196	Ade62196 Human Pro
12	11157.5	98.0	2161	7	ADE62200	Ade62200 Human Pro
13	11138.5	97.8	2161	2	AAR33545	Aar33545 Sequence
14	11036.5	96.9	2203	7	ADE62194	Ade62194 Rat Prote
15	11036.5	96.9	2203	7	ADD48697	Add48697 Rat Prote

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RESULT 5
AAR71002
ID   AAR71002 standard; protein; 2161 AA.
XX
AC   AAR71002;
XX
DT   25-MAR-2003  (revised)
DT   30-NOV-1995  (first entry)
XX
DE   Human neuronal calcium channel subunit alpha 1D including alternative.
DE   exon encoding the IS6 transmembrane domain.
XX
KW   Calcium channel subunit; antagonist; agonist; diagnosis;
KW   Lambert Eaton Syndrome.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 373. .406
FT                   /label= encoded by alternative exon
XX
PN   WO9504822-A1.
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XX
PD 16-FEB-1995.
XX
PF 11-AUG-1994; 94WO-US009230.
XX
PR 11-AUG-1993; 93US-00105536.
PR 05-NOV-1993; 93US-00149097.
XX
PA (SALK) SALK INST BIOTECHNOLOGY IND ASSOC.
XX
PI Harpold MM, Ellis SB, Williams ME, Mccue AF, Gillespie A;
XX
DR WPI; 1995-090900/12.
DR N-PSDB; AAQ84654.
XX
PT DNA encoding human calcium channel sub-unit(s) - used for developing
PT prods. for studying calcium channels, e.g. for obtaining agonists and
PT antagonists.
XX
PS Disclosure; Page 126-127; 285pp; English.
XX
CC The alpha 1D subunit cDNA has been isolated using fragments of the rabbit
CC skeletal muscle calcium channel alpha 1 subunit cDNA as a probe to screen
CC a cDNA library of human neuroblastoma cell line IMR32, to obtain clone
CC alpha1.36, This close was used as a probe to scren additional IMR32 cell
CC cDNa libraries to obtain overlapping clones, which were then employed for
CC screening until a sufficient series of clones to span the length of the
CC nt seuence encoding the human alpha 1D subunit was obtd. Full-length
CC clones were then constructed by ligating partial clones. AAQ84653 shows
CC the nt sequence of the cDNA encoding the alpha 1D subunit. The Alpha 1D
CC protein has a calculated Mr of 245,163. It contains four putative
CC internal repeated sequence regions which represent 24 putative
CC transmembrane segments. It mediates DHP-sensitive high-voltage, long-
CC lasting calcium channel activity. AAQ84654 shows an alternative exon
CC encoding the IS6 transmembrane domain. The difference occurs in AAs 373-
CC 406. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ Sequence 2161 AA;

Query Match 98.3%; Score 11202.5; DB 2; Length 2161;
Best Local Similarity 98.3%; Pred. No. 0;
Matches 2144; Conservative 1; Mismatches 1; Indels 35; Gaps 3;

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Qy          1 MMMMMMMKKMQHQRQQQADHANEANYARGTRLPLSGEGPTSQPNSSKQTVLSWQAAIDAA 60
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Db          1 MMMMMMMKKMQHQRQQQADHANEANYARGTRLPLSGEGPTSQPNSSKQTVLSWQAAIDAA 60

Qy         61 RQAKAAQTMSTSAPPPVGSLSQRKRQQYAKSKKQGNSSNSRPARALFCLSLNNPIRRACI 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 RQAKAAQTMSTSAPPPVGSLSQRKRQQYAKSKKQGNSSNSRPARALFCLSLNNPIRRACI 120

Qy        121 SIVEWKPFDIFILLAIFANCVALAIYIPFPEDDSNSTNHNLEKVEYAFLIIFTVETFLKI 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 SIVEWKPFDIFILLAIFANCVALAIYIPFPEDDSNSTNHNLEKVEYAFLIIFTVETFLKI 180

Qy        181 IAYGLLLHPNAYVRNGWNLLDFVIVIVGLFSVILEQLTKETEGGNHSSGKSGGFDVKALR 240
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Db        181 IAYGLLLHPNAYVRNGWNLLDFVIVIVGLFSVILEQLTKETEGGNHSSGKSGGFDVKALR 240

Qy        241 AFRVLRPLRLVSGVPSLQVVLNSIIKAMVPLLHIALLVLFVIIIYAIIGLELFIGKMHKT 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AFRVLRPLRLVSGVPSLQVVLNSIIKAMVPLLHIALLVLFVIIIYAIIGLELFIGKMHKT 300

Qy        301 CFFADSDIVAEEDPAPCAFSGNGRQCTANGTECRSGWVGPNGGITNFDNFAFAMLTVFQC 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 CFFADSDIVAEEDPAPCAFSGNGRQCTANGTECRSGWVGPNGGITNFDNFAFAMLTVFQC 360

Qy        361 ITMEGWTDVLYWVNDAIGWEWPWVYFVSLIILGSFFVLNLVLGVLSGEFSKEREKAKARG 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 ITMEGWTDVLYWVNDAIGWEWPWVYFVSLIILGSFFVLNLVLGVLSGEFSKEREKAKARG 420
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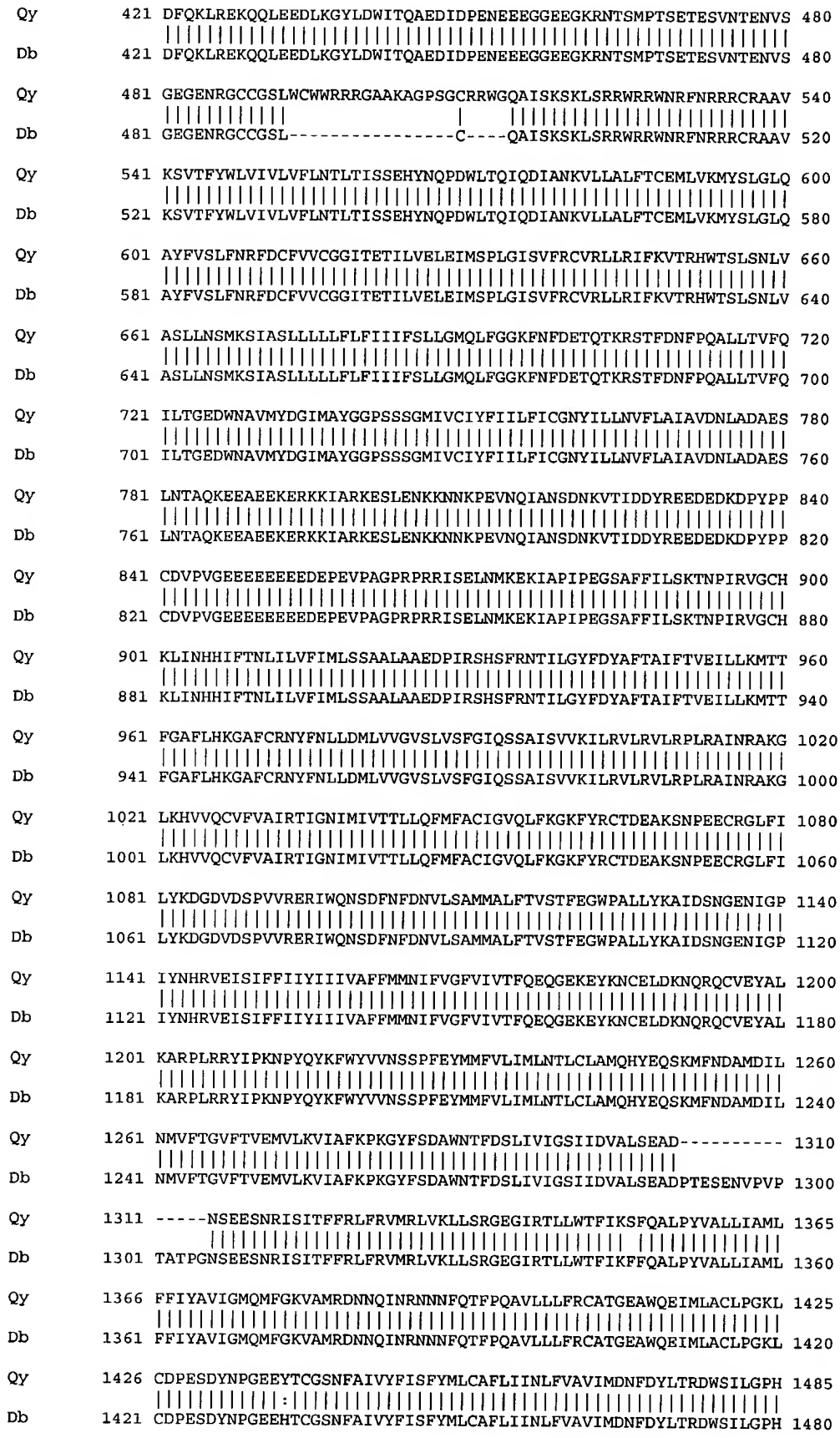

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Db       1481 HLDEFKRIWSEYDPEAKGRIKHLDVVTLLRRIQPPLGFGKLCPHRVACKRLVAMNMPLNS 1540

Qy       1546 DGTVMFNATLFALVRTALKIKTEGNLEQANEELRAVIKKIWKKTSMKLLDQVVPPAGDDE 1605
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1541 DGTVMFNATLFALVRTALKIKTEGNLEQANEELRAVIKKIWKKTSMKLLDQVVPPAGDDE 1600

Qy       1606 VTVGKFYATFLIQDYFRKFKKRKEQGLVGKYPAKNTTIALQAGLRTLHDIGPEIRRAISC 1665
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1601 VTVGKFYATFLIQDYFRKFKKRKEQGLVGKYPAKNTTIALQAGLRTLHDIGPEIRRAISC 1660

Qy       1666 DLQDDEPEETKREEEDDVFKRNGALLGNHVNHVNSDRRDSLQQTNTTHRPLHVQRPSIPP 1725
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1661 DLQDDEPEETKREEEDDVFKRNGALLGNHVNHVNSDRRDSLQQTNTTHRPLHVQRPSIPP 1720

Qy       1726 ASDTEKPLFPPAGNSVCHNHHNHNSIGKQVPTSTNANLNNANMSKAAHGKRPSIGNLEHV 1785
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1721 ASDTEKPLFPPAGNSVCHNHHNHNSIGKQVPTSTNANLNNANMSKAAHGKRPSIGNLEHV 1780

Qy       1786 SENGHHSSHKHDREPQRRSSVKRTRYYETYIRSDSGDEQLPTICREDPEIHGYFRDPHCL 1845
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1781 SENGHHSSHKHDREPQRRSSVKRTRYYETYIRSDSGDEQLPTICREDPEIHGYFRDPHCL 1840

Qy       1846 GEQEYFSSEECYEDDSSPTWSRQNYGYYSRYPGRNIDSERPRGYHHPQGFLEDDDSPVCY 1905
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1841 GEQEYFSSEECYEDDSSPTWSRQNYGYYSRYPGRNIDSERPRGYHHPQGFLEDDDSPVCY 1900

Qy       1906 DSRRSPRRRLLPPTPASHRRSSFNFECLRRQSSQEEVPSSPIFPHRTALPLHLMQQQIMA 1965
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1901 DSRRSPRRRLLPPTPASHRRSSFNFECLRRQSSQEEVPSSPIFPHRTALPLHLMQQQIMA 1960

Qy       1966 VAGLDSSKAQKYSPSHSTRSWATPPATPPYRDWTPCYTPLIQVEQSEALDQVNGSLPSLH 2025
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1961 VAGLDSSKAQKYSPSHSTRSWATPPATPPYRDWTPCYTPLIQVEQSEALDQVNGSLPSLH 2020

Qy       2026 RSSWYTDEPDISYRTFTPASLTVPSSFRNKNSDKQRSADSLVEAVLISEGLGRYARDPKF 2085
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Db       2021 RSSWYTDEPDISYRTFTPASLTVPSSFRNKNSDKQRSADSLVEAVLISEGLGRYARDPKF 2080

Qy       2086 VSATKHEIADACDLTIDEMESAASTLLNGNVRPRANGDVGPLSHRQDYELQDFGPGYSDE 2145
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Db       2081 VSATKHEIADACDLTIDEMESAASTLLNGNVRPRANGDVGPLSHRQDYELQDFGPGYSDE 2140

Qy       2146 EPDPGRDEEDLADEMICITTL 2166
             |||||||||||||||||||||
Db       2141 EPDPGRDEEDLADEMICITTL 2161
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RESULT 6
AAW63149
ID AAW63149 standard; protein; 2161 AA.
XX
AC AAW63149;
XX
DT 25-MAR-2003 (revised)
DT 12-OCT-1998 (first entry)
XX
DE Human calcium channel alpha-1D subunit.
XX
KW Alpha-1D subunit; human; calcium channel; assay; detection;
KW characterisation; Lambert Eaton Syndrome; LES; diagnosis.
XX
OS Homo sapiens.
XX
PN US5792846-A.
XX
PD 11-AUG-1998.
XX
PF 31-MAY-1995; 95US-00455543.

XX
PR 04-APR-1988; 88US-00176899.
PR 04-APR-1989; 89WO-US001408.
PR 20-FEB-1990; 90US-00482384.
PR 08-NOV-1990; 90US-00603751.
PR 30-NOV-1990; 90US-00620250.
PR 15-AUG-1991; 91US-00745206.
PR 04-APR-1994; 94US-00223305.
XX
PA (SIBI-) SIBIA NEUROSCIENCES INC.
XX
PI Brenner R, Ellis SB, Williams ME, Feldman DH, Mccue AF;
PI Harpold MM;
XX
DR WPI; 1998-456192/39.
DR N-PSDB; AAV42697.
XX
PT DNA encoding human calcium channel alpha 1B sub:unit protein - useful for
PT recombinant production of the channel for screening of its modulators,
PT and diagnosis of Lambert Eaton Syndrome.
XX
PS Disclosure; Col 271-284; 166pp; English.
XX
CC The present sequence represents the alpha-1D subunit of a human calcium
CC channel. Calcium channels are membrane-spanning, multi-subunit proteins
CC that allow controlled entry of calcium ions into cells. This leads to
CC depolarisation events required for muscle contraction. The recombinant
CC subunit, when expressed with nucleic acids encoding the complete calcium
CC channel, can be used in assays for the detection and characterisation of
CC compounds that modulate the channel. The DNA encoding the subunits can be
CC alternatively spliced when transcribed, giving more than one form of the
CC protein from the same transcript, each having slightly different
CC properties. In addition, the reactivity of the alpha 1 subunit with IgG
CC molecules from the serum of an individual with Lambert Eaton Syndrome
CC (LES) can be used as a diagnostic for the disease. (Updated on 25-MAR-
CC 2003 to correct PR field.)
XX
SQ Sequence 2161 AA;

Query Match 98.3%; Score 11202.5; DB 2; Length 2161;
Best Local Similarity 98.3%; Pred. No. 0;
Matches 2144; Conservative 1; Mismatches 1; Indels 35; Gaps 3;

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Qy         61 RQAKAAQTMSTSAPPPVGSLSQRKRQQYAKSKKQGNSSNSRPARALFCLSLNNPIRRACI 120
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Db         61 RQAKAAQTMSTSAPPPVGSLSQRKRQQYAKSKKQGNSSNSRPARALFCLSLNNPIRRACI 120

Qy        121 SIVEWKPFDIFILLAIFANCVALAIYIPFPEDDSNSTNHNLEKVEYAFLIIFTVETFLKI 180
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Db        121 SIVEWKPFDIFILLAIFANCVALAIYIPFPEDDSNSTNHNLEKVEYAFLIIFTVETFLKI 180

Qy        181 IAYGLLLHPNAYVRNGWNLLDFVIVIVGLFSVILEQLTKETEGGNHSSGKSGGFDVKALR 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 IAYGLLLHPNAYVRNGWNLLDFVIVIVGLFSVILEQLTKETEGGNHSSGKSGGFDVKALR 240

Qy        241 AFRVLRPLRLVSGVPSLQVVLNSIIKAMVPLLHIALLVLFVIIIYAIIGLELFIGKMHKT 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AFRVLRPLRLVSGVPSLQVVLNSIIKAMVPLLHIALLVLFVIIIYAIIGLELFIGKMHKT 300

Qy        301 CFFADSDIVAEEDPAPCAFSGNGRQCTANGTECRSGWVGPNGGITNFDNFAFAMLTVFQC 360
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Db        301 CFFADSDIVAEEDPAPCAFSGNGRQCTANGTECRSGWVGPNGGITNFDNFAFAMLTVFQC 360

Qy        361 ITMEGWTDVLYWVNDAIGWEWPWVYFVSLIILGSFFVLNLVLGVLSGEFSKEREKAKARG 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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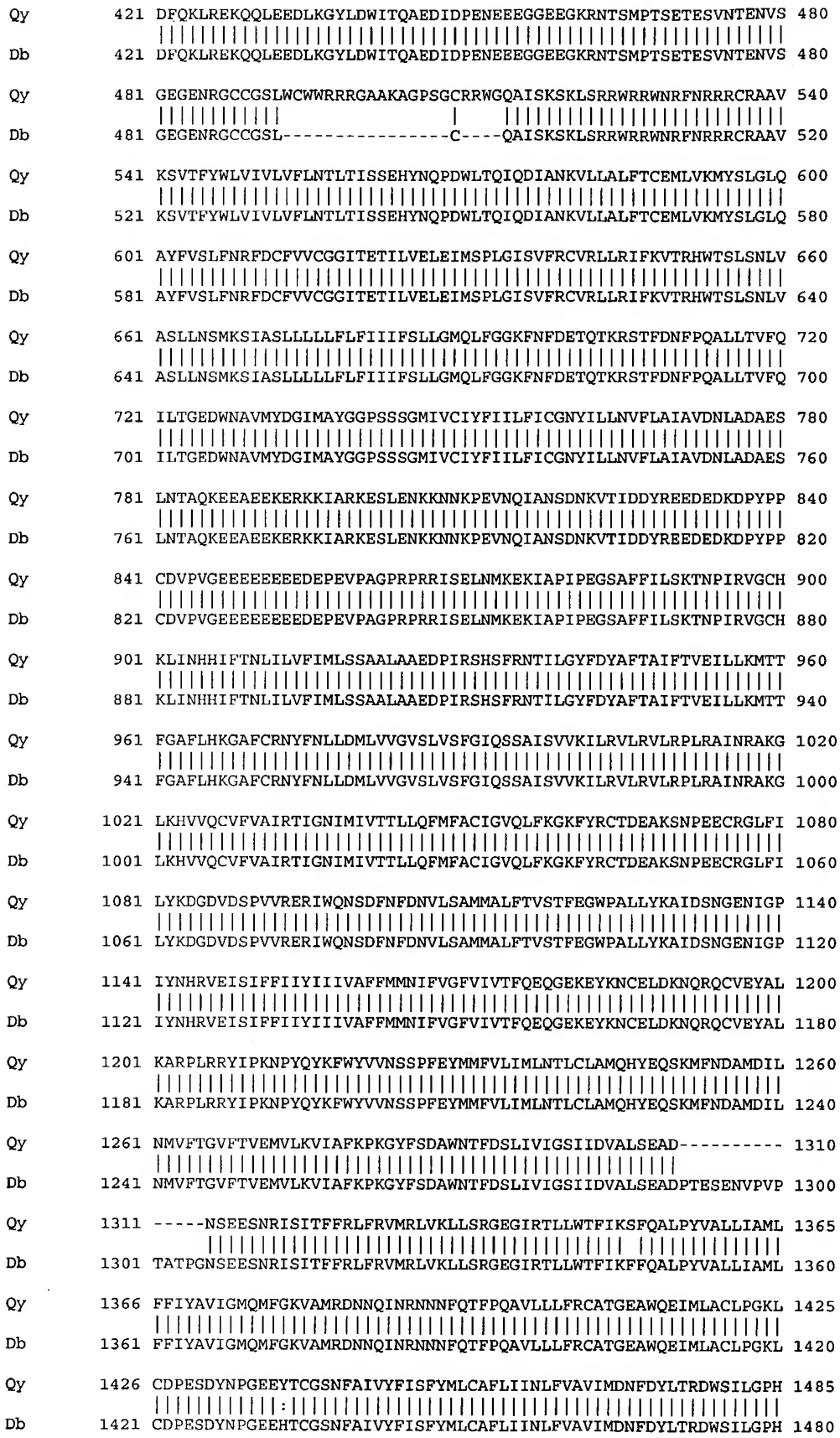

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Db       1481 HLDEFKRIWSEYDPEAKGRIKHLDVVTLLRRIQPPLGFGKLCPHRVACKRLVAMNMPLNS 1540

Qy       1546 DGTVMFNATLFALVRTALKIKTEGNLEQANEELRAVIKKIWKKTSMKLLDQVVPPAGDDE 1605
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Db       1541 DGTVMFNATLFALVRTALKIKTEGNLEQANEELRAVIKKIWKKTSMKLLDQVVPPAGDDE 1600

Qy       1606 VTVGKFYATFLIQDYFRKFKKRKEQGLVGKYPAKNTTIALQAGLRTLHDIGPEIRRAISC 1665
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1601 VTVGKFYATFLIQDYFRKFKKRKEQGLVGKYPAKNTTIALQAGLRTLHDIGPEIRRAISC 1660

Qy       1666 DLQDDEPEETKREEEDDVFKRNGALLGNHVNHVNSDRRDSLQQTNTTHRPLHVQRPSIPP 1725
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Db       1661 DLQDDEPEETKREEEDDVFKRNGALLGNHVNHVNSDRRDSLQQTNTTHRPLHVQRPSIPP 1720

Qy       1726 ASDTEKPLFPPAGNSVCHNHHNHNSIGKQVPTSTNANLNNANMSKAAHGKRPSIGNLEHV 1785
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Qy       1786 SENGHHSSHKHDREPQRRSSVKRTRYYETYIRSDSGDEQLPTICREDPEIHGYFRDPHCL 1845
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Qy       1846 GEQEYFSSEECYEDDSSPTWSRQNYGYYSRYPGRNIDSERPRGYHHPQGFLEDDDSPVCY 1905
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Db       1841 GEQEYFSSEECYEDDSSPTWSRQNYGYYSRYPGRNIDSERPRGYHHPQGFLEDDDSPVCY 1900

Qy       1906 DSRRSPRRRLLPPTPASHRRSSFNFECLRRQSSQEEVPSSPIFPHRTALPLHLMQQQIMA 1965
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Db       1961 VAGLDSSKAQKYSPSHSTRSWATPPATPPYRDWTPCYTPLIQVEQSEALDQVNGSLPSLH 2020

Qy       2026 RSSWYTDEPDISYRTFTPASLTVPSSFRNKNSDKQRSADSLVEAVLISEGLGRYARDPKF 2085
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Db       2021 RSSWYTDEPDISYRTFTPASLTVPSSFRNKNSDKQRSADSLVEAVLISEGLGRYARDPKF 2080

Qy       2086 VSATKHEIADACDLTIDEMESAASTLLNGNVRPRANGDVGPLSHRQDYELQDFGPGYSDE 2145
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Db       2081 VSATKHEIADACDLTIDEMESAASTLLNGNVRPRANGDVGPLSHRQDYELQDFGPGYSDE 2140

Qy       2146 EPDPGRDEEDLADEMICITTL 2166
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Db       2141 EPDPGRDEEDLADEMICITTL 2161
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RESULT 7
AAR71001
ID   AAR71001 standard; protein; 2161 AA.
XX
AC   AAR71001;
XX
DT   25-MAR-2003 (revised)
DT   30-NOV-1995 (first entry)
XX
DE   Human neuronal calcium channel subunit alpha 1D.
XX
KW   Calcium channel subunit; antagonist; agonist; diagnosis;
KW   Lambert Eaton Syndrome.
XX
OS   Homo sapiens.
XX
PN   WO9504822-A1.
XX
PD   16-FEB-1995.
XX
PF   11-AUG-1994;   94WO-US009230.

XX
PR 11-AUG-1993; 93US-00105536.
PR 05-NOV-1993; 93US-00149097.
XX
PA (SALK) SALK INST BIOTECHNOLOGY IND ASSOC.
XX
PI Harpold MM, Ellis SB, Williams ME, Mccue AF, Gillespie A;
XX
DR WPI; 1995-090900/12.
DR N-PSDB; AAQ84653.
XX
PT DNA encoding human calcium channel sub-unit(s) - used for developing
PT prods. for studying calcium channels, e.g. for obtaining agonists and
PT antagonists.
XX
PS Disclosure; Page 116-126; 285pp; English.
XX
CC The alpha 1D subunit cDNA has been isolated using fragments of the rabbit
CC skeletal muscle calcium channel alpha 1 subunit cDNA as a probe to screen
CC a cDNA library of human neuroblastoma cell line IMR32, to obtain clone
CC alpha1.36, This close was used as a probe to scren additional IMR32 cell
CC cDNa libraries to obtain overlapping clones, which were then employed for
CC screening until a sufficient series of clones to span the length of the
CC nt seuence encoding the human alpha 1D subunit was obtd. Full-length
CC clones were then constructed by ligating partial clones. AAQ84653 shows
CC the nt sequence of the cDNA encoding the alpha 1D subunit. The Alpha 1D
CC protein has a calculated Mr of 245,163. It contains four putative
CC internal repeated sequence regions which represent 24 putative
CC transmembrane segments. It mediates DHP-sensitive high-voltage, long-
CC lasting calcium channel activity. (Updated on 25-MAR-2003 to correct PN
CC field.)
XX
SQ Sequence 2161 AA;

Query Match 98.0%; Score 11168.5; DB 2; Length 2161;
Best Local Similarity 98.0%; Pred. No. 0;
Matches 2138; Conservative 5; Mismatches 3; Indels 35; Gaps 3;

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Qy         61 RQAKAAQTMSTSAPPPVGSLSQRKRQQYAKSKKQGNSSNSRPARALFCLSLNNPIRRACI 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 RQAKAAQTMSTSAPPPVGSLSQRKRQQYAKSKKQGNSSNSRPARALFCLSLNNPIRRACI 120

Qy        121 SIVEWKPFDIFILLAIFANCVALAIYIPFPEDDSNSTNHNLEKVEYAFLIIFTVETFLKI 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 SIVEWKPFDIFILLAIFANCVALAIYIPFPEDDSNSTNHNLEKVEYAFLIIFTVETFLKI 180

Qy        181 IAYGLLLHPNAYVRNGWNLLDFVIVIVGLFSVILEQLTKETEGGNHSSGKSGGFDVKALR 240
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Db        181 IAYGLLLHPNAYVRNGWNLLDFVIVIVGLFSVILEQLTKETEGGNHSSGKSGGFDVKALR 240

Qy        241 AFRVLRPLRLVSGVPSLQVVLNSIIKAMVPLLHIALLVLFVIIIYAIIGLELFIGKMHKT 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AFRVLRPLRLVSGVPSLQVVLNSIIKAMVPLLHIALLVLFVIIIYAIIGLELFIGKMHKT 300

Qy        301 CFFADSDIVAEEDPAPCAFSGNGRQCTANGTECRSGWVGPNGGITNFDNFAFAMLTVFQC 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 CFFADSDIVAEEDPAPCAFSGNGRQCTANGTECRSGWVGPNGGITNFDNFAFAMLTVFQC 360

Qy        361 ITMEGWTDVLYWVNDAIGWEWPWVYFVSLIILGSFFVLNLVLGVLSGEFSKEREKAKARG 420
              |||||||||||:|||:|:| ||||||||:| ||||||||||||||||||||||||||||||
Db        361 ITMEGWTDVLYWMNDAMGFELPWVYFVSLVIFGSFFVLNLVLGVLSGEFSKEREKAKARG 420

Qy        421 DFQKLREKQQLEEDLKGYLDWITQAEDIDPENEEEGGEEGKRNTSMPTSETESVNTENVS 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 DFQKLREKQQLEEDLKGYLDWITQAEDIDPENEEEGGEEGKRNTSMPTSETESVNTENVS 480

Qy        481 GEGENRGCCGSLWCWWRRRGAAKAGPSGCRRWGQAISKSKLSRRWRRWNRFNRRRCRAAV 540
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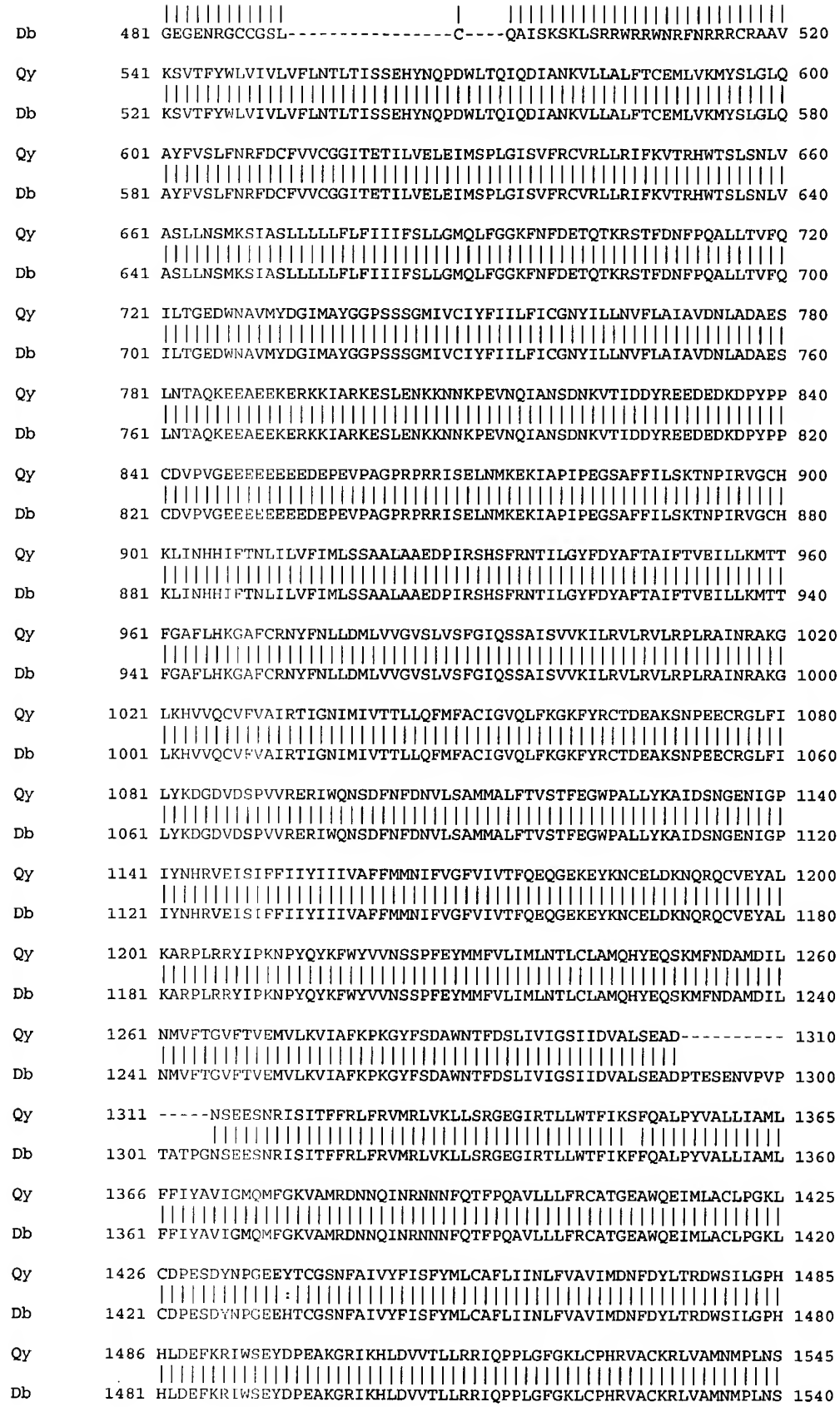

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Qy       1546 DGTVMFNATLFALVRTALKIKTEGNLEQANEELRAVIKKIWKKTSMKLLDQVVPPAGDDE 1605
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Db       1541 DGTVMFNATLFALVRTALKIKTEGNLEQANEELRAVIKKIWKKTSMKLLDQVVPPAGDDE 1600

Qy       1606 VTVGKFYATFLIQDYFRKFKKRKEQGLVGKYPAKNTTIALQAGLRTLHDIGPEIRRAISC 1665
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1601 VTVGKFYATFLIQDYFRKFKKRKEQGLVGKYPAKNTTIALQAGLRTLHDIGPEIRRAISC 1660

Qy       1666 DLQDDEPEETKREEEDDVFKRNGALLGNHVNHVNSDRRDSLQQTNTTHRPLHVQRPSIPP 1725
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Db       1661 DLQDDEPEETKREEEDDVFKRNGALLGNHVNHVNSDRRDSLQQTNTTHRPLHVQRPSIPP 1720

Qy       1726 ASDTEKPLFPPAGNSVCHNHHNHNSIGKQVPTSTNANLNNANMSKAAHGKRPSIGNLEHV 1785
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1721 ASDTEKPLFPPAGNSVCHNHHNHNSIGKQVPTSTNANLNNANMSKAAHGKRPSIGNLEHV 1780

Qy       1786 SENGHHSSHKHDREPQRRSSVKRTRYYETYIRSDSGDEQLPTICREDPEIHGYFRDPHCL 1845
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1781 SENGHHSSHKHDREPQRRSSVKRTRYYETYIRSDSGDEQLPTICREDPEIHGYFRDPHCL 1840

Qy       1846 GEQEYFSSEECYEDDSSPTWSRQNYGYYSRYPGRNIDSERPRGYHHPQGFLEDDDSPVCY 1905
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1841 GEQEYFSSEECYEDDSSPTWSRQNYGYYSRYPGRNIDSERPRGYHHPQGFLEDDDSPVCY 1900

Qy       1906 DSRRSPRRRLLPPTPASHRRSSFNFECLRRQSSQEEVPSSPIFPHRTALPLHLMQQQIMA 1965
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1901 DSRRSPRRRLLPPTPASHRRSSFNFECLRRQSSQEEVPSSPIFPHRTALPLHLMQQQIMA 1960

Qy       1966 VAGLDSSKAQKYSPSHSTRSWATPPATPPYRDWTPCYTPLIQVEQSEALDQVNGSLPSLH 2025
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1961 VAGLDSSKAQKYSPSHSTRSWATPPATPPYRDWTPCYTPLIQVEQSEALDQVNGSLPSLH 2020

Qy       2026 RSSWYTDEPDISYRTFTPASLTVPSSFRNKNSDKQRSADSLVEAVLISEGLGRYARDPKF 2085
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Db       2021 RSSWYTDEPDISYRTFTPASLTVPSSFRNKNSDKQRSADSLVEAVLISEGLGRYARDPKF 2080

Qy       2086 VSATKHEIADACDLTIDEMESAASTLLNGNVRPRANGDVGPLSHRQDYELQDFGPGYSDE 2145
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2081 VSATKHEIADACDLTIDEMESAASTLLNGNVRPRANGDVGPLSHRQDYELQDFGPGYSDE 2140

Qy       2146 EPDPGRDEEDLADEMICITTL 2166
              |||||||||||||||||||||
Db       2141 EPDPGRDEEDLADEMICITTL 2161
```

Sequence Comparison B
SEQ ID NO: 4

```
RESULT 5
AAR71002
ID   AAR71002 standard; protein; 2161 AA.
XX
AC   AAR71002;
XX
DT   25-MAR-2003  (revised)
DT   30-NOV-1995  (first entry)
XX
DE   Human neuronal calcium channel subunit alpha 1D including alternative.
DE   exon encoding the IS6 transmembrane domain.
XX
KW   Calcium channel subunit; antagonist; agonist; diagnosis;
KW   Lambert Eaton Syndrome.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 373. .406
FT                   /label= encoded by alternative exon
XX
PN   WO9504822-A1.
XX
PD   16-FEB-1995.
XX
PF   11-AUG-1994;   94WO-US009230.
XX
PR   11-AUG-1993;   93US-00105536.
PR   05-NOV-1993;   93US-00149097.
XX
PA   (SALK ) SALK INST BIOTECHNOLOGY IND ASSOC.
XX
PI   Harpold MM,  Ellis SB,  Williams ME,  Mccue AF,  Gillespie A;
XX
DR   WPI; 1995-090900/12.
DR   N-PSDB; AAQ84654.
XX
PT   DNA encoding human calcium channel sub-unit(s) - used for developing
PT   prods. for studying calcium channels, e.g. for obtaining agonists and
PT   antagonists.
XX
PS   Disclosure; Page 126-127; 285pp; English.
XX
CC   The alpha 1D subunit cDNA has been isolated using fragments of the rabbit
CC   skeletal muscle calcium channel alpha 1 subunit cDNA as a probe to screen
CC   a cDNA library of human neuroblastoma cell line IMR32, to obtain clone
CC   alpha1.36, This close was used as a probe to scren additional IMR32 cell
CC   cDNa libraries to obtain overlapping clones, which were then employed for
CC   screening until a sufficient series of clones to span the length of the
CC   nt seuence encoding the human alpha 1D subunit was obtd. Full-length
CC   clones were then constructed by ligating partial clones. AAQ84653 shows
CC   the nt sequence of the cDNA encoding the alpha 1D subunit. The Alpha 1D
CC   protein has a calculated Mr of 245,163. It contains four putative
CC   internal repeated sequence regions which represent 24 putative
CC   transmembrane segments. It mediates DHP-sensitive high-voltage, long-
CC   lasting calcium channel activity. AAQ84654 shows an alternative exon
CC   encoding the IS6 transmembrane domain. The difference occurs in AAs 373-
CC   406. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence 2161 AA;

  Query Match             98.3%;  Score 11202.5;  DB 2;  Length 2161;
  Best Local Similarity   98.3%;  Pred. No. 0;
  Matches 2144;  Conservative    1;  Mismatches    1;  Indels   35;  Gaps    3;
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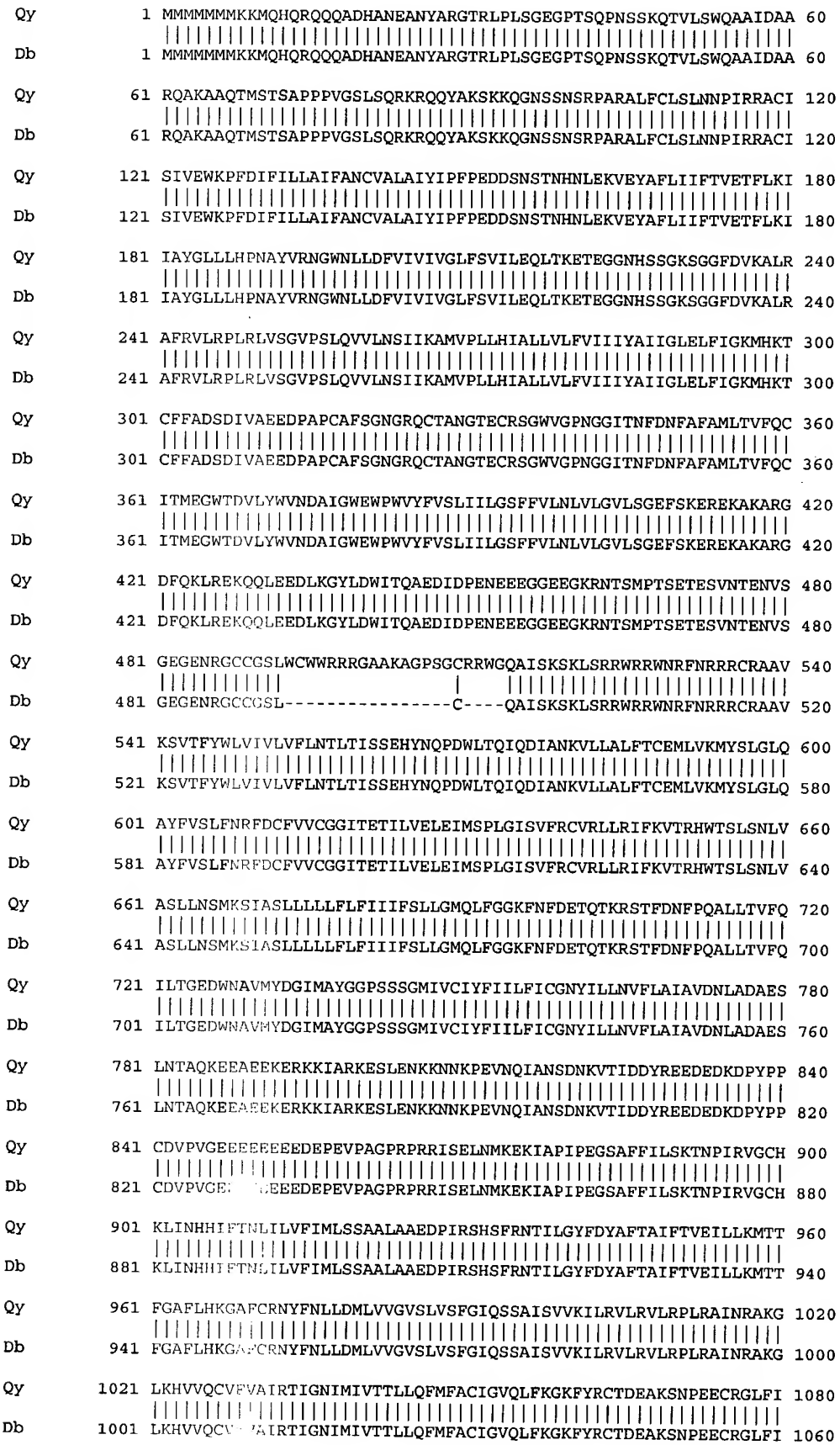

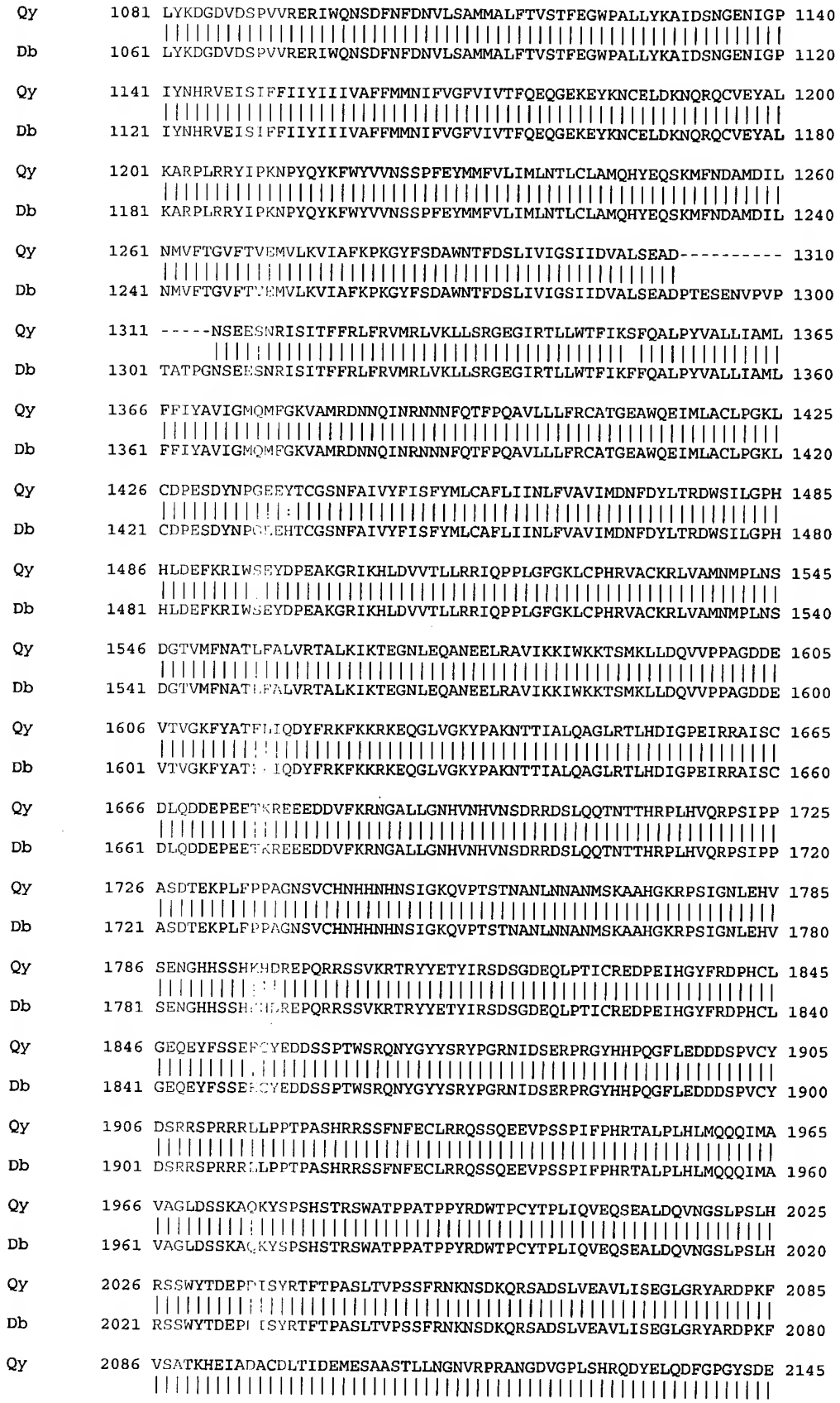

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Db       2081 VSATKHEIADACDLTIDEMESAASTLLNGNVRPRANGDVGPLSHRQDYELQDFGPGYSDE 2140

Qy       2146 EPDPGRDEEDLADEMICITTL 2166
              |||||||||||||||||||||
Db       2141 EPDPGRDEEDLADEMICITTL 2161
```